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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/965,553	09/27/2001	David A. Wright	900.175US2	5748

26191 7590 03/12/2004

FISH & RICHARDSON P.C.
3300 DAIN RAUSCHER PLAZA
60 SOUTH SIXTH STREET
MINNEAPOLIS, MN 55402

EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 03/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/965,553	WRIGHT ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50-56,60,69-72 and 108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50-56,60,69-72 and 108* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. The objection to the specification is withdrawn, in light of insertion of sequence identifiers in the appropriate locations.

3. The rejection of claims 77 and 78 under 35 U.S.C. 112, 2nd paragraph is withdrawn in light of the claim cancellations.

4. The rejection of claim 49 under 35 U.S.C. 102(b) is withdrawn in light of the claim cancellation.

Double Patenting

5. Claims 50, 52-56, and 69-71 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 6,331,662 ('662), for the reasons of stated in the Office action mailed August 27, 2003.

In the paper submitted December 29, 2003, Applicants state that a terminal disclaimer will be submitted upon an indication that the claims of the present application are otherwise allowable (response, page 10, 2nd full paragraph). Applicants' intent is acknowledged.

6. Claim 56 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/315,515 ('515), for the reasons of stated in the Office action mailed August 27, 2003.

In the paper submitted December 29, 2003, Applicants state that a terminal disclaimer will be submitted upon an indication that the claims of the present application are otherwise allowable (response, page 10, 2nd full paragraph). Applicants' intent is acknowledged.

Claim Rejections - 35 USC § 112

7. Claims 50-56, 60, 69-72, and 108 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of stated in the Office action mailed August 27, 2003. Applicants traverse the rejection in the paper filed December 29, 2003. Applicants' arguments have been fully considered but were not found persuasive.

Applicants argue that, in contrast to the specification at issue in *University of California v. Eli Lilly*, the present specification discloses five embodiments of nucleotide sequences that contain a primer binding sites at least 95% identical to SEQ ID NO: 1 or 2, nine embodiments of a reverse transcriptase coding sequence at least 70% identical to SEQ ID NO: 11, and six embodiments of a long terminal repeat. Applicants argue that SEQ ID NOs: 17, 19, and 23 contain all three elements, with the long terminal repeat positioned 5' to the primer binding site

or 3' to the reverse transcriptase coding sequence (response, page 11, 2nd full paragraph and the paragraph bridging pages 11-12).

However, the isolated nucleic acids encompassed by the claims also comprise other sequences. SEQ ID NOs: 1 and 2 are each 18 bases long. The generic reverse transcriptase coding sequence of SEQ ID NO: 11 is 600 bases long. The Athila reverse transcriptase coding sequence of SEQ ID NO: 27 is 180 bases long. The Cyclops and Calypso reverse transcriptase coding sequences of SEQ ID NOs: 29 and 34 are both 597 bases long. Yet, the claimed isolated nucleic acids comprise a nucleotide sequence that is at a minimum about 4906 bases long and up to about 12,571 bases long, and also comprise at least one long terminal repeat. The structures and functions of the other sequences of the claimed isolated nucleic acids have not been described, and are not limited by the claims in any manner. The genus of claimed isolated nucleic acids therefore encompasses rather widely varying species. Applicants indicate that the specification discloses SEQ ID NOs: 17, 19, and 23 as three embodiments of the claimed nucleic acid. However, as broadly interpreted, the claimed nucleic acids can comprise sequences, other than the SEQ ID NO: 1, SEQ ID NO: 2, and the reverse transcriptase coding sequence, that do not have the same functions as the sequences of SEQ ID NOs: 17, 19, and 23. SEQ ID NOs: 17, 19, and 23 therefore are not representative of the widely varying genus of isolated nucleic acids encompassed by the claims, as the claimed nucleic acids can have functions that are not encompassed by SEQ ID NOs: 17, 19, and 23.

Further, the sequences that make up long terminal repeats are also not disclosed in the specification. Applicants in their arguments indicate that SEQ ID NOs: 17 and 19-23 are embodiments of long terminal repeats (response, page 11, 2nd full paragraph). However, the

summary of the sequence listing on pages 19-20 of the specification indicates that these sequences retroelements, and the sequences that make up the long terminal repeats are not disclosed. Furthermore, claim 50 does not limit the reverse transcriptase coding sequence to have any level of sequence identity to SEQ ID NO: 11.

7. Claims 50-56, 60, 69-72, and 108 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for SEQ ID NO: 17, does not reasonably provide enablement for other isolated nucleic acids comprising a primer binding site selected from a sequence having at least 95% identity to SEQ ID NO: 1 or SEQ ID NO: 2, a reverse transcriptase coding sequence positioned 3' to said primer binding site, and at least one long terminal repeat positioned 5' to said primer binding site or 3' to said reverse transcriptase coding sequence, vectors that can transfer nucleic acids to plant cells comprising the claimed isolated nucleic acids, and a method to transfer nucleic acid into a plant cell, comprising contacting the claimed nucleic acids with at least one plant cell. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection replaces the scope of enablement rejection presented in the Office action mailed August 27, 2003, due to the claim amendments.

The specification indicates that the Calypso-1, -2, and -3 retroelements were aligned using the ClustalX v1.63b program to generate a consensus sequence. The amino acid sequence encoded by the consensus sequence was determined and compared to amino acid sequences of retrovirus-like elements from soybean, pea (Cyclops2), and *Athila*-like elements of Arabidopsis.

A new consensus sequence was determined for the coding regions of the protease, reverse transcriptase, and integrase (pages 56-57, Example 4). A summary of the sequence listing on pages 19-20 indicates that SEQ ID NOs: 1 and 2 are specialized primer binding site versions 1 and 2, respectively, that SEQ ID NO: 11 is the nucleic acid of a generic reverse transcriptase, the amino acid sequence of which is set forth in SEQ ID NO: 12, and that SEQ ID NO: 17 is a generic retroelement.

However, the specification does not teach other isolated nucleic acids encompassed by the claims. The claims broadly encompass any and all nucleic acids having any function, as long as they comprise the limitations of parts (a)-(c) of claim 50 or parts (a)-(d) of claim 69. However, the specification does not teach all such isolated nucleic acids. The identities, and therefore the functions, of the sequences that make up the remainder of the claimed nucleic acids are unknown. It is then unclear, and not taught by the specification, how one skilled in the art is to use the claimed nucleic acids. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

The specification also does not teach nucleic acid sequences that have at least 70% identity with SEQ ID NO: 11 or which encode amino acid sequences having at least 79% identity with SEQ ID NO: 12. The specification does not teach what amino acid sequences of SEQ ID NO: 12 may be changed without affecting its reverse transcriptase activity. The specification indicates that the generic reverse transcriptase coding sequence was determined by "best matching the coding information in all elements" (page 56, lines 32-34). However, the specification does not teach what changes can be made to the consensus sequence of the reverse

transcriptase of SEQ ID NO: 12 without affecting functional activity. In the absence of further guidance, undue experimentation would be required by one skilled in the art to make nucleotide sequences that differ from SEQ ID NO: 11 by as much as 30%, or which encode an amino acid sequence that differs from SEQ ID NO: 12 by as much as 12%, while retaining the functional activity of SEQ ID NO: 12.

Further, the specification does not enable the claimed vectors, or claimed method. As SEQ ID NOs: 1 and 2 are primer binding sites, and SEQ ID NO: 12 is a reverse transcriptase, it is unclear how one would use plant cells that were transformed a nucleic acid comprising these sequences and at least one long terminal repeat, when the identity of the remaining sequences is unknown, nor is this explained in the specification. The specification prophetically indicates that methods are provided to transfer nucleic acids into plant cells, comprising contacting a plant retroelement with a plant cell (page 14). The specification prophetically indicates that a generic retroelement will be modified so that it will express at high levels in plant cells, and because the modified generic element will be expressed at high levels, retroviral particles will be produced by the host plant cell, which will be incubated in the presence of non-transformed plant cells, and that the virus will associate with the plant cell and fuse with the cell membrane (page 57). However, the specification does not teach that any retroelement was successfully used to transfer nucleic acids of interest into plant cells. Peterson-Burch et al. teach that the role of env-like open reading frames of plant retroviruses can *now* be tested (page 152, emphasis added). Vicient et al. (Genome Research, 2001, Vol. 11, pages 2041-2049) assert that, while ENV of Bagy-2 and other retrotransposons are active, that the question of function remains uncertain, and that a replication or infection-competent plant errantivirus must be identified and its life cycle characterized in

order to resolve the question of ENV function in plants (page 2046). These teachings indicate that further basic research is required before one skilled in the art can use the claimed nucleic acids with the claimed vectors and with the claimed method. Wright et al. (Genome Research, 2001, Vol. 12, pages 122-131) also stress that "The identification of a replication-competent *Athila* group element will be necessary to test the hypothesis that these elements are infectious plant retroviruses. *If* this proves to be the case, the *Athila* group elements *may* be useful as vectors for gene transfer and the genetic modification of plants" (page 130, emphases added). This also indicates that the claimed invention was not enabled at the time the instant application was filed, and that further research is required to enable the claimed invention. In the absence of further guidance, undue experimentation would be required to use the claimed vectors or practice the claimed method. Given the breadth of the claims, unpredictability of the art, and lack of guidance of the specification, as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Applicants' arguments will be addressed as they apply to the rejection. While admitting that claims 50 and 69 cover a number of embodiments, Applicants argue that they include relevant limitations, such as a specified size range for the nucleic acid, a primer binding site having 95% sequence identity to SEQ ID NO: 1 or 2, a reverse transcriptase coding sequence, and long terminal repeats, and particular arrangements of these sequences (response, paragraph bridging pages 12-13). However, the function of the remaining sequences of the claimed nucleic acid is unknown. It is not clear how one skilled in the art is to use nucleic acid sequences whose identity is unknown. It is not clear what the relationship of the primer binding site, reverse

transcriptase coding sequence, and long terminal repeat is to the other, unidentified nucleotide sequences.

Applicants argue that one skilled in the art would have been able to use standard molecular biology techniques to prepare the claimed nucleic acids. Applicants argue that retroelement motifs such as long terminal repeats, reverse transcriptase coding sequences, and primer binding sites are known in the art (response, page 13, last paragraph). However, the claims do not indicate that the isolated nucleic acids form a retroelement, or that any of the recited components are from retroelements. Applicants continue, arguing that the specification provides sufficient guidance for making the claimed nucleic acid molecules, and that SEQ ID NOs: 17, 19, and 23 are examples (response, page 14, 1st full paragraph). However, it is noted that SEQ ID NOs: 17, 19, and 23 are retroelements, whereas the claims do not limit the nucleic acids to be retroelements. Further, as discussed in the last Office action, the specification does not teach that any retroelements, or the claimed nucleic acids, were actually transferred into plant cells. Also as previously discussed, the teachings of the prior art indicate that further basic research is required to determine if retroelements can be used as vectors to transfer nucleic acids into plant cells.

Applicants argue that the specification teaches that nucleic acids can be used as primers or probes (response, page 14, 1st full paragraph). However, this is not a specific utility. Applicants argue that the specification teaches that the nucleic acids can be incorporated into a vector and delivered to host cells (response, page 14, 1st full paragraph). However, the specification does not teach how one is to use a nucleic acid molecule that comprises a primer binding site and a reverse transcriptase coding sequence. The identity of the other sequences

present on the nucleic acid is unknown. Further, as discussed above, the specification does not enable the use of retroelements as vectors. Applicants also argue that one skilled in the art would have appreciated that the claimed nucleic acid molecules could be used as markers for molecular breeding, and cite several references that demonstrate the use of known plant retroelements in molecular breeding (response, page 14, 1st full paragraph). However, the claims do not limit the nucleic acids to be retroelements. Further, SEQ ID NO: 17, for example, is a generic retroelement, and SEQ ID NO: 11 is a generic reverse transcriptase coding sequence. The specification does not teach how one would use the claimed nucleic acids for this purpose.

Summary

8. Claims 50-56, 60, 69-72, and 108 remain rejected.

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ashwin Mehta whose telephone number is 571-272-0803. The examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

March 9, 2004

Ashwin D. Mehta, Ph.D.
Primary Examiner
Art Unit 1638